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09/554,024	10/16/2000	Georges Freyssinet	33207-PCT-US	6532

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EXAMINER
IBRAHIM, MEDINA AHMED

ART UNIT	PAPER NUMBER
1638	13

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/554,024	Applicant(s) FREYSSINET ET AL.	
	Examiner Medina Ibrahim	Art Unit 1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 April 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) *10-12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9 and 13-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restriction

1. Applicants' election without traverse of Group I, claims 1-9 and 13-30, in Paper No.11 is acknowledged. The restriction is made FINAL.

Claims 1-30 are pending.

Claims 1-9 and 13-30 are under examination.

Claims 10-12 are withdrawn from consideration as being drawn to a non-elected invention.

Sequence Listing

Applicant's CRF and paper sequence listing have been entered.

Information Disclosure Statement

Initialed and dated copy of Applicant's IDS form 1449, Paper No 6 is attached to the instant Office action.

Drawings

2. This drawing filed with this application are approved by the Draftsperson.

Objections

Claims 3-4 and 8 are objected to because of the following informalities: A claim should not have more than one period.

The pathogen species in claim 25 should be italicized. Appropriate correction is required.

Claim Rejections - 35 USC § 112, 2nd paragraph

3. Claims 1-9 and 13-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 1-2, 5, and 8-9, "characterized in that it" is not a US- recognized term. It is suggested that "characterized in that it" be replaced with --wherein said nucleic acid fragment--.

In claims 2-9, "Nucleic acid fragment" should be changed to ---The nucleic acid fragment---, for proper dependency.

In claims 2-4, what does a "DNA-type nucleotide sequence" mean?

In claims 3-4 and 8, "homologous" is unclear as to the degree of homology. The specification defines the degree of homology as " at least 70%, 80%, or 90% relative to the reference sequence". However, it is unclear as to whether the homology is based on functional or structural homology. If the latter is intended, it is unclear if the structural homology is based on sequence identity (entire sequence) or sequence similarity (a portion) or both. While clarification is required, new matter should be avoided. Also, "described by the sequence identifier No.1 (SEQ ID NO1)" should be replaced with ---of SEQ ID NO:1---; and "the" before "said" be deleted, for clarification.

In claim 5, "fused" doesn't define an operable linkage. Also, "and/or" is indefinite. Is the nucleotide sequence in addition to SEQ ID NO:1? If so, the claim should read ---further comprising a second nucleotide sequence--. What is a "protein-thanatin"? Protein is generally

defined as a sequence with more than 100 amino acid residues, while peptide is a sequence with 3 to 100 amino acid residues. So, if thanatin is not a protein, how can the signal peptide be? Also, it is unclear how can a fusion protein be obtained if the nucleic acid is fused in the 3' to the sequence encoding thanatin.

Claim 6 is confusing in the recitation of "the protein is a signal peptide or transit peptide".

In claim 7, "the signal peptide is the signal peptide of" should be replaced with ---- the signal peptide is from---. Also, "the tobacco PR1a gene" implies that there is only one tobacco PR1a gene. It is unclear if there is only one tobacco PR1a gene.

In claims 3-4, 6-7, 13-14, and 22, "characterized in that" should be replaced with --- wherein ---.

In claim 13,"as well as" should be replaced with ---and---, for clarification.

4. A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex*

parte Hall, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claims 13 and 28 recite the broad recitation host organism, and the claim also recites plant which is the narrower statement of the range/limitation. Claim 25 recites the broad recitations of *Ceroscospora, Cladosporium, Fusarium, and Phytophthora* , and the narrower limitations of *Ceroscospora beticola, Cladosporium herbarum Fusarium graminaream, Fusarium culmorum , and Phytophthora cinamomi.* Correction is required

In claims 14 and 15, "Chimeric gene" should be changed to ---The chimeric gene---, for proper dependency.

Claim 14 recites an improper Markush group.

In claim 15, "characterized in that it" should be replaced with ----wherein the chimeric gene---.

In claim 16, "characterized in that it" should be replaced with ---wherein said cloning or expression vector---, for clarification.

In claims 17-18, "characterized in that it" should be replaced with---wherein said vector--, for clarification. Also, "Vector" should be changed to ---The cloning or the expression vector---, for proper dependency.

In claim 17, what is a "developed plant"? "its" refers to what?

In claim 19, "characterized in that they" should be replaced with ----wherein said host organisms---, for clarification. What is "an effective quantity' of a chimeric gene. The "a" before "chimeric gene" should be replaced with ---the---, for proper dependency.

In claims 20-21, "characterized in that it" should be replaced with ---wherein said host organism---, for clarification. Also, "Transformed" should be changed to---The transformed---, for proper dependency.

In claim 20, it is unclear what is "transformed host organism that consists plant cells or plants.

In claim 21, "Transformed host organism"(singular) lacks antecedence basis in claim 20, which recites "Transformed host organisms" (plural).

In claim 22, "Host" should be changed to---The host----, for proper dependency.

In claim 23, "characterized in that it" should be replaced with ---wherein said plant cell---, for clarification. Also, "a nucleic acid" should be changed to ---the nucleic acid---, for proper dependency.

In claims 24-26 and "characterized in that it " should be replaced with ---- wherein said plant---.

In claims 24 and 25, "Transformed plant" should be changed to ---A transformed plant--- and ---The transformed plant---, for proper article and proper dependency, respectively.

In claim 26, "derived " is indefinite as it is unclear what is being retained in the derived plant. Also, "and/or" renders the claim indefinite. Also "plants"(plural) lacks antecedence basis in claim 24. Also "either of" before "claim 24" should be deleted, for clarification.

Claim 27 is indefinite as it is unclear whether the seeds from the transformed plant of claim 24 retain the nucleic acid fragment. It is suggested that ----, wherein said seeds retain the nucleic acid fragment--- be inserted before the period.

Claims 28-30 are incomplete method steps. Also, "characterized in that" should be replaced with ---whereby-----.

In claims 28, "the" before "said" should be deleted.

In claim 30, "the chimeric gene" lacks antecedence basis in claim 28. Also, "by means" renders the claim indefinite as it lacks function.

The claims are replete with vague and indefinite terms. A careful and complete review of all claims are suggested.

Claim Rejections 35 USC § 101

Claims 1-9 and 19-30 are rejected under 35 U.S.C. 101 because the nucleic acid fragment of claim 1 is directed to a non-isolated and naturally occurring nucleic acid fragment. It is suggested that "Nucleic acid" of claim 1 be changed to ---An isolated nucleic acid---. Claim 19 is drawn to transformed host organisms which reads on human organisms which is a non-statutory subject matter and cannot be patented. It is suggested that "organism" be replaced with ---plant---- or ---host cell---

Claim Rejections - 35 USC § 112, Scope of Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any

person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention

Claims 1-9 and 13-30 are rejected under 35 U.S.C. 112, first paragraph, because the specification while being enabling for the nucleic acid fragment of SEQ ID NO:1, from *Psodius maculiventis*, encoding thanatin with bactericidal or fungicidal properties when expressed in transformed plants or the synthetic sequence of SEQ ID NO: 2 or 5, does not provide enablement for any nucleic fragment from any source encoding thanatin, homologous or complementary sequences of SEQ ID NO:1, 2, or 5 encoding thanatin, non-plant host organisms or their transformation methods, or method of transforming plants for bacterial or fungal resistance using non-exemplified sequences. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make/use the invention commensurate in scope with these claims.

Claims broadly drawn to a nucleic acid fragment encoding thanatin, vector comprising it, transformed non-plant host organisms, and method for making transformed plants with resistance against any disease, or homologous or complementary sequences of SEQ ID NO:1, 2 or 5 are not supported by an enabling disclosure. The specification only provides

guidance for the isolated nucleic acid fragment of SEQ ID NO:1, 2 or 5 encoding antifungal and antibacterial peptides, transformed plant expressing said sequence, and a method for producing said plants. The specification does not provide any guidance for the identification and obtention of all DNA sequence encoding thanatin which may be useful in the production of transformed plants with resistance to all and any plant diseases. No specific guidance has been provided for probe/prime sequences, hybridization, and wash conditions to obtain any and all nucleic acid fragment encoding thanatin. It is unclear whether *Psodius maculiventis* is the only source of thanatin or whether it can also be obtained from other natural sources. If the latter is true, it is unclear how one skilled in the art would be able to identify and isolate a nucleic acid fragment encoding thanatin from a vast pool of natural sources and determine which nucleic acid(s) would be the desired ones, other than by random trial and error requiring undue experimentation.

The specification is not enabling for the claims drawn to homologous (as defined in page 5 of the specification) sequences because neither the instant specification nor the prior art discloses or provides guidance as to where in the nucleic acid fragment encoding thanatin can be modified so as the thanatin activity is retained. It is unpredictable whether

any modifications in SEQ ID NO:1 or 5 will retain the thanatin activity. The state of the art as exemplified by Fehlbaum et al (PNAS, vol. 93, pp. 1221-1225, 1996) that one or few amino acid modifications in thanatin can drastically reduce its activity against many bacteria and fungi pathogens (see page 1223, Table 1). Therefore, it is unpredictable if any and all homologous sequences of the disclosed sequences would have any antimicrobial activity. Regarding the claims that recite complementary sequences, the claims read on sequences that are not fully complementary which encompass as few as 2-mer. It is unlikely that a sequence with 2-mer would have any function.

Regarding claims 24 and 26, the specification does not disclose or provide guidance for a DNA sequence, disclosed or non-disclosed, that is capable of rendering a plant resistant to all or any diseases. There is no known DNA/protein that provides universal resistance in a plant against all pathogens including all nematodes, aphids, fungi, bacteria, and viruses. Ryals et al (The Plant Cell, 1996, page 1809, 2nd full paragraph) teach unpredictability in the expression of non-race specific genes in conferring a broad spectrum of disease resistance in tobacco plants. The only working examples disclosed in the specification are limited transformed plants

expressing SEQ ID NO:1. No transgenic plant with disease resistance has been disclosed or evaluated.

Therefore, given the lack of guidance, the state of the prior art, the nature of the invention, the unpredictability, and scope of the claims as discussed above, the instant invention cannot be practiced without undue experimentation, absent further guidance.

See Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ 2d 1016 at 1021 and 1027, (Fed. Cir. 1991) at page 1021, where it is taught that a gene is not reduced to practice until the inventor can define it by "its physical or chemical properties" (e.g a DNA sequence) and page 1027, where it is taught that the disclosure of a few gene sequences did not enable claims broadly drawn to any analog thereof.

Written Description

Claims 1-9 and 13-30 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to all nucleic acid fragments from any source encoding thanatin, transformed host organisms and transformed disease

resistant plant, homologous or complementary sequences of SEQ ID NO:1, 2 or 5 and a method for transforming plants. Applicants disclosed SEQ ID NO:1, 2 or 5 encoding thanatin and transformed plants expressing SEQ ID NO:1. This is a genus claim. The specification does not set forth any specific physical or chemical characteristics or any other relevant identifying characteristics for other thanatin encoding nucleic acid molecules. The specification does not provide any specific chemical or physical characteristics for each of the claimed homologous or complementary sequences, and a review of literature does not indicate that such characteristics would be well known by a skilled artisan. There is known correlation between the structure and function of thanatin DNA/protein. Since no specific sequence identification or any other relevant property have been disclosed for all DNA encoding thanatin, a person skilled in the art would not recognize from the disclosure that Applicant was in possession of the invention as broadly claimed. See, Written Description Examination Guidelines published in Federal Registry/Vol. 66, No.4/Friday, January 5, 2001/Notices). See, also *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997), which teaches that the disclosure of a process for obtaining cDNA from a particular organism and the description of the encoded protein fail

to provide an adequate written description of the actual cDNA from that organism which would encode the protein from that organism, despite the disclosure of a cDNA encoding that protein from another organism.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-9 and 13-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mitsuhara et al (EP 0798 381 A2, Applicant's IDS) in

view of Fehlabaum et al (PNAS, vol. 93, pp. 1221-1225, 1996, Applicant's IDS).

Claims are drawn any nucleic acid fragment including homologous or complementary sequences of SEQ ID NO:1, 2 or 5 encoding thanatin, expression vector comprising heterologous regulatory elements including a signal peptide from tobacco PR1a gene, fungal or bacterial-resistant transformed plants or plant cells comprising said thanatin sequences, and methods for producing said transformed plants/plant cells.

Mitsuhara et al teach an isolated gene, from Diptera insect encoding antibacterial and antifungal peptide, in a plasmid or recombinant expression vector comprising heterologous 5' and 3' regulatory elements including the signal peptide of tobacco PR-1a gene (pages 6-7, Example 1), methods for producing bacterial and fungal resistant transformed plants comprising expressing said gene in said plants (page 8, Example 3), and transformed tobacco plants resistant to phytophthora infections (page 11, Example 10).

Mutsahara et al do not teach thanatin DNA/peptide.

Fehlbaum et al disclosed an isolated and purified thanatin from *Psodius macuiventris* having bactericidal and fungicidal activity, and

methods of synthesizing thanatin derivatives with a wide range of antimicrobial activity.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the method of producing disease-resistant transformed plants as taught by Mitsuhara et al, and to modify that method by incorporating any other antimicrobial peptide, like the thanatin disclosed by Fehlbaum et al, given the knowledge of one of skilled in the art for how to obtain the nucleotide sequence encoding the disclosed thanatin, to produce transformed plants with resistance to microbial diseases as taught by Mitsuhara et al, with reasonable expectation of success. One skilled in the art would have been motivated to use thanatin because of its antimicrobial effects as taught by Fehlbaum and its availability. In addition, Applicants have not shown any unexpected results from the use of a viral vector. Thus, the claimed invention as whole was clearly *prima facie* obvious.

Remarks

No claim is allowed.

Papers relating to this application may be submitted to Technology Sector 1 by facsimile transmission. Papers should be faxed to Crystal Mall 1, Art Unit 1638, using fax number (703) 308-4242. All Technology Sector 1 fax machines are available to receive transmissions 24 hrs/day, 7 days/wk. Please note that the faxing of such papers must conform with the

Notice published in the Official Gazette, 1096 OG 30, (November 15, 1989).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Medina a. Ibrahim whose telephone number is (703) 306-5822. The Examiner can normally be reached Monday -Tuesday from 8:00AM to 4:00PM and Wednesday-Thursday from 9:00AM to 3:00 PM .

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Amy Nelson, can be reached at (703) 306-3218.

Any inquiry of a general nature or relating to the status of this application should be directed to the receptionist whose telephone number is (703) 308-0196.

July 2, 2002

mai

ELIZABETH F. McELWAIN
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